Quantitative Analysis of the Effect of Dementia Status on the Progression of Brain Volume Loss and Cognitive Decline Over Time

1. Introduction

Alzheimer's disease and other forms of dementia are among the most pressing health challenges of our time, with a significant impact on individuals, families, and healthcare systems around the world. Alzheimer's disease is currently ranked as the seventh leading cause of death in the United States and the most common cause of dementia in older adults (National Institute on Aging).

This report offers a detailed exploration and quantitative analysis utilizing data from the open-access Imaging Research Series (INF2178_A4_data.csv). This dataset, amassed through repeated measurements, records cognition in individuals potentially experiencing various stages of dementia. Based on these data, a pertinent research question emerges:

1. **Research Question:** How does dementia status influence the progression of brain volume loss and cognitive decline over time?

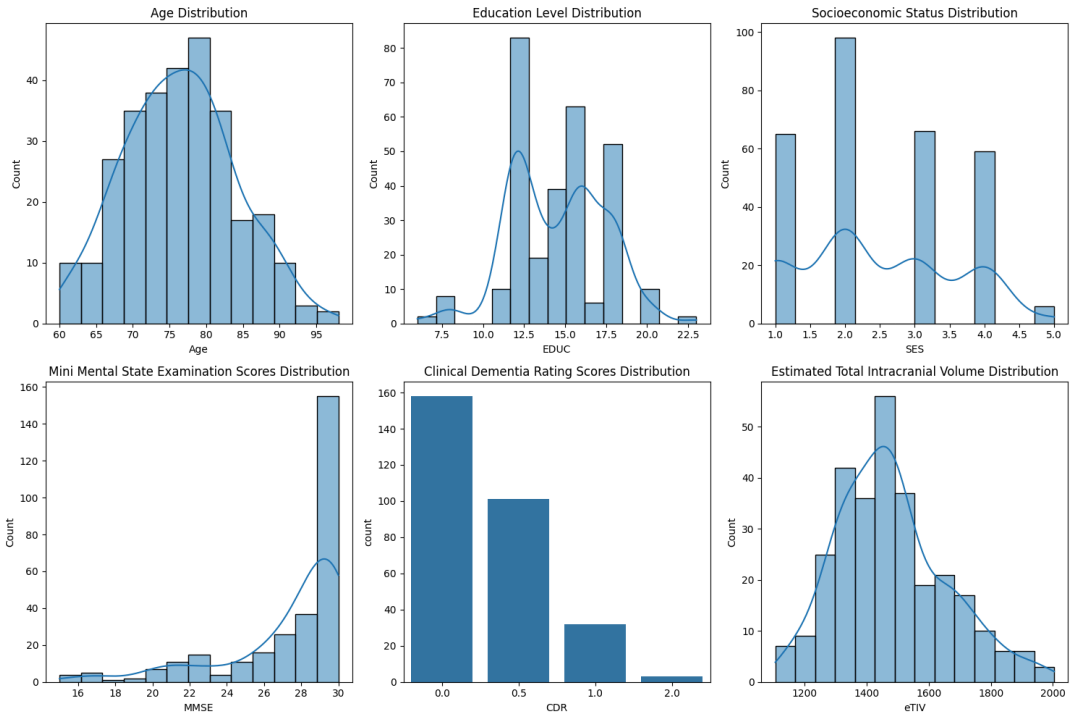
This question aims to investigate the connection between dementia and the observed changes in brain volume and cognitive function.

2. Data Cleaning

The SES column contains 15 missing values, and the MMSE column has one missing value. Given that the dataset comprises only 294 rows, we will employ the mode to fill in these missing values. This approach helps preserve certain characteristics of the original data.

3. EDA

Data Visualization



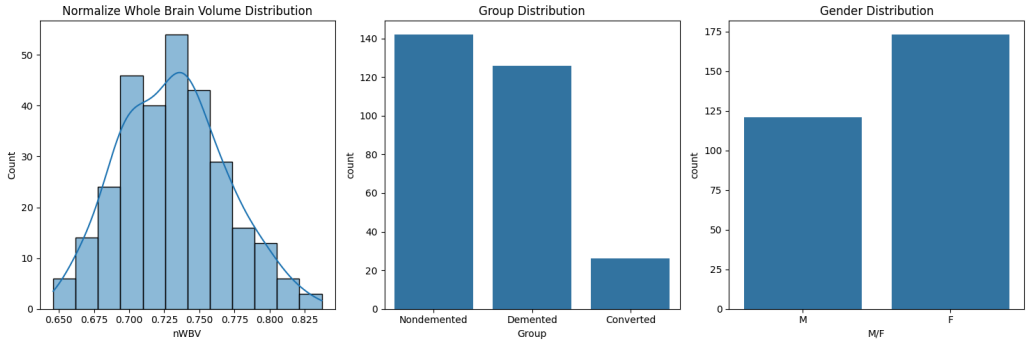


Figure 1: Exploratory Data Analysis

Based on Figure 1, it is evident that the age distribution among the subjects is uniform, primarily spanning from middle-aged to elderly individuals. The majority of these subjects have received between 12 to 18 years of education, with a notable concentration around 12 years, reflecting variances in educational backgrounds. The Mini-Mental State Examination (MMSE) scores predominantly lean towards the higher end, suggesting that a significant portion of the subjects either had no or mild cognitive impairment. Clinical Dementia Rating (CDR) scores were mainly scored at 0, indicating an absence of dementia, although there were instances of higher impairment levels. This score is a categorical variable used to gauge the severity of dementia. The estimated total intracranial volume (eTIV) showcased a broad distribution, pointing to differences in brain size among subjects. Additionally, the number of non-demented individuals surpassed those with dementia, providing a comparative group for exploring the impact of dementia.

4. Mixed Effects Anova

Aov_nwbv

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ANOVA SUMMARY
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Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	0.034	2	141	0.017	6.712	0.002	0.087	nan
Visit	0.007	1	141	0.007	94.251	0.000	0.401	1.000
Interaction	0.000	2	141	0.000	1.534	0.219	0.021	nan

Table 1: Aov_nwbv ANOVA Summary

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POST HOC TESTS
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Contrast	Visit	A	B	Paired	Parametric	T	dof	alternative	p-unc	p-corr	p-adjust	BF10	hedges
Visit	-	1	2	True	True	9.672	143.000	two-sided	0.000	nan	nan	225800000000000.000	0.255
Group	-	Converted	Demented	False	True	1.401	14.676	two-sided	0.182	0.546	bonf	0.668	0.469
Group	-	Converted	Nondemented	False	True	-0.648	15.832	two-sided	0.527	1.000	bonf	0.361	-0.188
Group	-	Demented	Nondemented	False	True	-3.690	129.436	two-sided	0.000	0.001	bonf	75.094	-0.633
Visit * Group	1	Converted	Demented	False	True	1.444	14.626	two-sided	0.170	1.000	bonf	0.701	0.486
Visit * Group	1	Converted	Nondemented	False	True	-0.465	15.995	two-sided	0.648	1.000	bonf	0.333	-0.134
Visit * Group	1	Demented	Nondemented	False	True	-3.413	129.011	two-sided	0.001	0.005	bonf	32.393	-0.584
Visit * Group	2	Converted	Demented	False	True	1.324	14.879	two-sided	0.205	1.000	bonf	0.615	0.436
Visit * Group	2	Converted	Nondemented	False	True	-0.811	15.615	two-sided	0.429	1.000	bonf	0.397	-0.240
Visit * Group	2	Demented	Nondemented	False	True	-3.856	129.952	two-sided	0.000	0.001	bonf	127.576	-0.663

Table 2: Aov_nwbv Post Hoc Test

As shown in Table 1 and Table 2, there was a significant difference in normalized whole brain volume (nWBV) between groups (p = 0.002), indicating that dementia status has an impact on brain volume. Additionally, nWBV changed significantly over time (p < 0.001), demonstrating that brain volume is affected over time.

Aov_mmse

ANOVA SUMMARY

Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	1313.469	2	141	656.735	55.470	0.000	0.440	nan
Visit	20.587	1	141	20.587	8.033	0.005	0.054	1.000
Interaction	15.549	2	141	7.774	3.033	0.051	0.041	nan

Table 3: Aov_mmse ANOVA Summary

POST HOC TESTS

Contrast	Visit	A	B	Paired	Parametric	T	dof	alternative	p-unc	p-corr	p-adjust	BF10	hedges
Visit	-	1	2	True	True	2.795	143.000	two-sided	0.006	nan	nan	3.872	0.156
Group	-	Converted	Demented	False	True	6.710	50.636	two-sided	0.000	0.000	bonf	1911000.000	1.157
Group	-	Converted	Nondemented	False	True	-1.303	12.315	two-sided	0.216	0.649	bonf	0.599	-0.584
Group	-	Demented	Nondemented	False	True	-9.458	65.491	two-sided	0.000	0.000	bonf	24630000000000.000	-1.735
Visit * Group	1	Converted	Demented	False	True	8.076	60.165	two-sided	0.000	0.000	bonf	447900000.000	1.319
Visit * Group	1	Converted	Nondemented	False	True	0.489	13.999	two-sided	0.633	1.000	bonf	0.336	0.167
Visit * Group	1	Demented	Nondemented	False	True	-9.124	68.185	two-sided	0.000	0.000	bonf	3993000000000.000	-1.669
Visit * Group	2	Converted	Demented	False	True	4.469	33.632	two-sided	0.000	0.001	bonf	599.356	0.879
Visit * Group	2	Converted	Nondemented	False	True	-1.816	11.802	two-sided	0.095	0.570	bonf	1.126	-0.937
Visit * Group	2	Demented	Nondemented	False	True	-8.385	66.088	two-sided	0.000	0.000	bonf	76510000000.000	-1.537

Table 4: Aov_mmse Post Hoc Test

As shown in Table 3 and Table 4, a significant group effect (p < 0.001) indicates that cognitive function differs between groups. Additionally, there was a significant change in Mini-Mental State Examination (MMSE) scores from the first to the second visit (p = 0.005), indicating changes in cognitive function over time. Furthermore, the interaction effect approached significance (p = 0.051), suggesting that further data may reveal variations in how cognitive function changes over time across different groups.

Aov_etiv

ANOVA SUMMARY

Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	37424.708	2	141	18712.354	0.297	0.743	0.004	nan
Visit	5573.920	1	141	5573.920	9.225	0.003	0.061	1.000
Interaction	1004.783	2	141	502.392	0.831	0.438	0.012	nan

Table 5: Aov_etiv ANOVA Summary

POST HOC TESTS

Contrast	Visit	A	B	Paired	Parametric	T	dof	alternative	p-unc	p-corr	p-adjust	BF10	hedges
Visit	-	1	2	True	True	-3.041	143.000	two-sided	0.003	nan	nan	7.532	-0.049
Group	-	Converted	Demented	False	True	-0.897	17.630	two-sided	0.382	1.000	bonf	0.423	-0.249
Group	-	Converted	Nondemented	False	True	-0.796	17.491	two-sided	0.437	1.000	bonf	0.393	-0.210
Group	-	Demented	Nondemented	False	True	0.159	129.303	two-sided	0.874	1.000	bonf	0.189	0.027
Visit * Group	1	Converted	Demented	False	True	-0.863	18.004	two-sided	0.400	1.000	bonf	0.413	-0.235
Visit * Group	1	Converted	Nondemented	False	True	-0.845	17.676	two-sided	0.409	1.000	bonf	0.406	-0.221
Visit * Group	1	Demented	Nondemented	False	True	0.034	129.047	two-sided	0.973	1.000	bonf	0.187	0.006
Visit * Group	2	Converted	Demented	False	True	-0.927	17.492	two-sided	0.367	1.000	bonf	0.432	-0.258
Visit * Group	2	Converted	Nondemented	False	True	-0.747	17.368	two-sided	0.465	1.000	bonf	0.382	-0.199
Visit * Group	2	Demented	Nondemented	False	True	0.280	129.320	two-sided	0.780	1.000	bonf	0.193	0.048

Table 6: Aov_etiv Post Hoc Test

As shown in Table 5 and Table 6, there is no significant group effect (p = 0.743), suggesting that intracranial volume does not depend on group classification. Additionally, there was a significant change in estimated total intracranial volume (eTIV) from the first to the second visit (p = 0.003), indicating changes in intracranial volume over time. The absence of a significant interaction (p = 0.438) means that changes in intracranial volume over time did not differ between groups.

These mixed-effects ANOVA analyses provide important insights into the dynamics of dementia's effects on brain volume and cognitive function. The analysis showed significant differences in standardized whole-brain volume and Mini-Mental State Examination scores between groups differentiated by dementia status, highlighting the far-reaching impact of the disease. Notably, nWBV and MMSE scores decreased over time in all groups. In contrast, estimated intracranial volume (eTIV) showed no between-group differences, suggesting that it is less sensitive to dementia status than nWBV and cognitive function.

Sample size

In order to explore the impact of different income groups on students' reading and math test scores over time, controlling for fall general knowledge scores as a covariate, an OLS Regression Model is fitted, and here are the key findings:

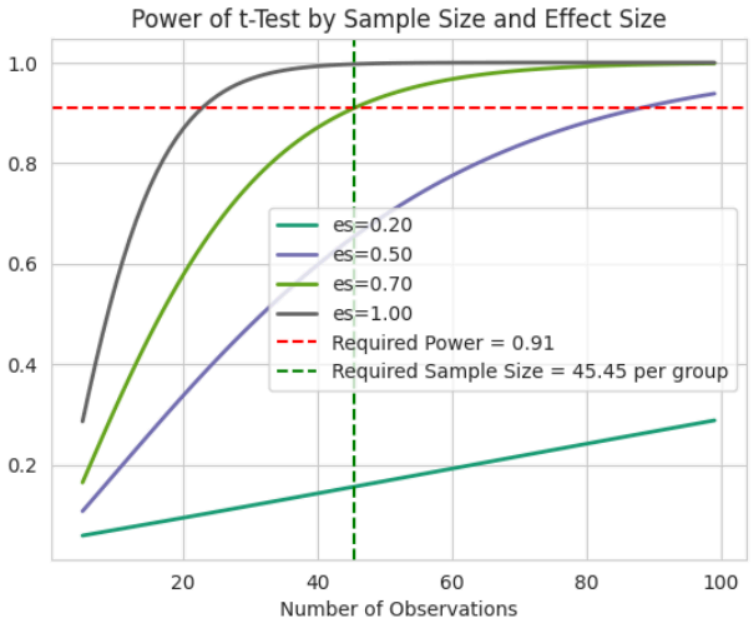

Figure 2: Power of T-Test by Sample Size and Effect Size

To achieve the specified statistical analysis goals with a power of 0.91, an alpha of 0.05, and an effect size of 0.7, the theoretical average number of samples required for each group is calculated to be 45.45, which rounds up to 46. This number ensures that the study has sufficient power to detect existing effects, while also avoiding the waste of resources and enhancing the credibility of the study.

5. Reference

Alzheimer's Disease fact Sheet. (April 05, 2023). National Institute on Aging. https://www.nia.nih.gov/health/alzheimers-and-dementia/alzheimers-disease-fact-sheet